CLAIMS

What is claimed is:

1. A method for detecting the presence of an analyte in a solution, wherein said analyte comprises at least two mutually exclusive recognition sites that are capable of binding to corresponding mutually exclusive recognition molecules, said method comprising the steps of:

a) providing a first sensor that comprises a first recognition molecule that is capable of binding to one of said recognition sites on said analyte, said first sensor further comprising a first enzyme portion that is attached to said first recognition molecule;

b) providing a second sensor that comprises a second recognition molecule that is capable of binding to another of said recognition sites on said analyte, said second sensor further comprising a second enzyme portion that is attached to said second recognition molecule;

c) mixing said first sensor and said second sensor with a solution that may or may not contain said analyte, wherein said recognition sites on said analyte comprises at least a first recognition site and a second recognition site, said first recognition site being capable of binding to said first sensor and said second recognition site being capable of binding to said second sensor and wherein said first recognition site and second recognition site are located within said analyte such that said first enzyme portion and said second enzyme portion combine to form a biologically active enzyme when said first and second recognition molecules bind to said first and second recognition sites; and

d) detecting if said biologically active enzyme has been formed to thereby provide detection of the presence of said analyte in said solution.

2. A method for detecting the presence of an analyte in a solution according to claim 1 wherein said target analyte is selected from the group consisting of protein, DNA, RNA, lipids and sugars.
3. A method for detecting the presence of an analyte in a solution according to claim 2 wherein said protein is an antigen.
4. A method for detecting the presence of an analyte in a solution according to claim 1 wherein said first and second recognition molecules are selected from the group consisting of single chain antibody fragments, antibody fragments, full antibodies, DNA oligomers, DNA aptamers and PNA oligomers .
5. A method for detecting the presence of an analyte in a solution according to claim 2 wherein said recognition molecule is a single chain antibody fragment, antibody fragment or a full antibody.
6. A method for detecting the presence of an analyte in a solution according to claim 4 wherein said analyte is DNA or RNA and said recognition molecule is a DNA oligomer, DNA aptamer or PNA oligomer .
7. A method for detecting the presence of an analyte in a solution according to claim 1 wherein said biologically active enzyme is selected from the group consisting of renilla luciferase, B-lactomase and B-galactosidase.
8. A method for detecting the presence of an analyte in a solution according to claim 1wherein said step of detecting if said biologically active enzyme has been formed comprises the steps of reacting said biologically active enzyme with a first reactant to form a first product and detecting the presence of said first product in said solution to thereby provide detection of the presence of said analyte in said solution.
9. A method for detecting the presence of an analyte in a solution according to claim 8 wherein said first product is an activator of a second enzyme and wherein said step of detecting if said biologically active enzyme has been formed comprises the additional steps of:

a) reacting said second enzyme with said first product to form an activated amplifier enzyme;

b) reacting said activated amplifier enzyme with a second reactant to form a second product; and

c) detecting the presence of said second product in said solution to thereby provide detection of the presence of said analyte in said solution.

10. A method for detecting the presence of an analyte according to claim 1 wherein said analyte is located on or in a cell.

11. A method of making an analyte detection system which includes split enzyme biosensors, the method comprising:

a) selecting an analyte with two mutually exclusive recognition sites;

b) selecting two recognition molecules corresponding to the recognition sites; and

c) adding complementary enzyme portions to the two recognition molecules to form said split enzyme biosensors.

12. A method of splitting an enzyme into two functionally complementary portions with reconstituted enzyme activity, the method comprising:

a) splitting the enzyme into two portions;

b) cyclically mutating the two portions;

c) expressing the two portions in the same cell;

d) adding substrate; and

e) selecting cells with reconstituted enzyme activity.

13. A method of making a sensor for a target analyte, the method comprising:

a) choosing a portion of a split enzyme;

b) linking the split enzyme to a target binding domain;

c) randomly mutating the a target binding domain to generate a library; and

d) screening the library for affinity to the target analyte.